

Listing of Claims

1-32. (Canceled)

33. (Currently Amended) A non-human transgenic animal expressing a molecule of claim 24 N- and C-terminally double truncated type IA tau molecule, type IB tau molecule, type IIA tau molecule, or type IIB tau molecule.

34. (Previously Presented) A method of screening or testing a candidate compound for utility in the treatment of Alzheimer's disease comprising obtaining a non-human transgenic animal according to claim 33 and using the animal to screen or test the candidate compound.

35. (New) The non-human transgenic animal of claim 33, wherein the non-human transgenic animal expresses a type IA tau molecule:

having at least the first 236 N-terminal amino acids and at least the last 45 C-terminal amino acids of the 4 repeat containing tau43 truncated;
detectable in Alzheimer's diseased brain tissue but not detectable in normal healthy brain tissue; and
preventing normal tau protein from promoting microtubule assembly in an in vitro microtubule assembly assay, wherein prevention of the promotion of microtubule assembly can be eliminated by specific inhibitory, neutralizing monoclonal antibodies against the molecules in a microtubule assembly assay.

36. (New) The non-human transgenic animal of claim 35, wherein the type IA tau molecule comprises an amino acid sequence of any of SEQ ID NO: 1 to 3.

37. (New) The non-human transgenic animal of claim 34, wherein the non-human transgenic animal expresses a type IB tau molecule:

having at least the first 238 N-terminal amino acids and at least the last 40 C-terminal amino acids of the 4 repeat containing tau43 or the first 207 N-terminal amino acids and at least the last 50 C-terminal amino acids of the 3 repeat containing tau44 truncated;
detectable in Alzheimer's diseased brain tissue whereas the molecules are not detectable in normal healthy brain tissue; and

not capable of preventing wild type tau from promoting microtubule assembly in an in vitro microtubule assembly assay.

38. (New) The non-human transgenic animal of claim 37, wherein the type IB tau molecule comprises an amino acid sequence of any of SEQ ID NO: 4 to 10.

39. (New) The non-human transgenic animal of claim 34, wherein the non-human transgenic animal expresses a type IIA tau molecule:

having at least the first 68 N-terminal amino acids and at least the last 40 C-terminal amino acids of the 4 repeat containing tau43 or the first 68 N-terminal amino acids and at least the last 20 C-terminal amino acids of the 3 repeat containing tau44 truncated;

detectable in Alzheimer's diseased brain tissue, whereas the molecules are not detectable in normal healthy brain tissue;

having higher microtubule assembly promoting activity than wild type tau in an in vitro microtubule assembly assay, wherein the microtubule assembly promoting activity can be eliminated by specific inhibitory, neutralizing monoclonal antibodies against the molecules in a microtubule assembly assay; and

wherein pathologic activity of the molecule relies on binding to the microtubular network defined by the microtubule polymerization promoting activity.

40. (New) The non-human transgenic animal of claim 39, wherein the type IIA tau molecule comprises the amino acid sequence of any of SEQ ID NO: 11 to 18.

41. (New) The non-human transgenic animal of claim 34, wherein the non-human transgenic animal expresses a type IIB tau molecule:

having at least the first 68 N-terminal amino acids and at least the last 40 C-terminal amino acids of the 4 repeat containing tau43 or the first 68 N-terminal amino acids and at least the last 20 C-terminal amino acids of the 3 repeat containing tau44 truncated;

detectable in Alzheimer's diseased brain tissue, whereas the molecules are not detectable in normal healthy brain tissue; and

having a pathological microtubule assembly promoting activity different from wild type tau in an in vitro microtubule assembly assay.

42. (New) The non-human transgenic animal of claim 41, wherein the type IIB tau molecule comprises the amino acid sequence of any of SEQ ID NO: 19 to 20.